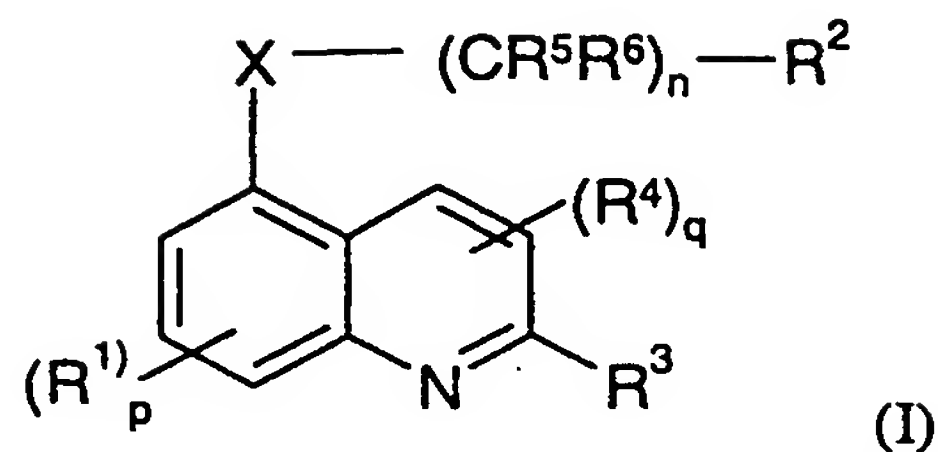


CLAIMS

1. A compound of formula



5 or a pharmaceutically acceptable salt or solvate thereof, wherein

p is 0, 1 or 2;

each R¹ independently represents halogen or C₁-C₆ alkyl optionally substituted by at least one substituent selected from hydroxyl, halogen and C₁-C₆ alkoxy;

X is C(O)NH or NHC(O);

10 n is 1, 2, 3, 4 or 5;

within each grouping, CR⁵R⁶, R⁵ and R⁶ each independently represent hydrogen, halogen, phenyl or C₁-C₆ alkyl, or R⁵ and R⁶ together with the carbon atom to which they are both attached form a C₃-C₈ cycloalkyl ring;

R² represents an unsaturated 4- to 10-membered ring system which may comprise at least one ring heteroatom selected from nitrogen, oxygen and sulphur, the ring system being optionally substituted with at least one substituent selected from halogen, -COOR¹³, hydroxyl, -NR¹⁴R¹⁵, -CONR¹⁶R¹⁷, -SO₂NR¹⁸R¹⁹, -NR²⁰SO₂R²¹, C₁-C₆ alkyl, C₁-C₆ alkylcarbonyl, C₁-C₆ alkoxy, C₁-C₆ alkylcarbonyloxy, C₁-C₆ alkoxy carbonyl, C₁-C₆ hydroxyalkyl and -S(O)_mC₁-C₆ alkyl where m is 0, 1 or 2;

20 R³ represents hydrogen or a group -R⁷, -OR⁷, -SR⁷ or -NR⁷R⁸;

q is 0, 1 or 2;

each R⁴ independently represents halogen or C₁-C₆ alkyl optionally substituted by at least one substituent selected from hydroxyl, halogen and C₁-C₆ alkoxy;

R⁷ and R⁸ each independently represent hydrogen, C₁-C₁₀ alkyl, C₃-C₈ cycloalkyl or a saturated or unsaturated 3- to 10-membered heterocyclic ring system comprising at least one ring heteroatom selected from nitrogen, oxygen and sulphur, the alkyl, cycloalkyl and heterocyclic ring system each being optionally substituted with at least one substituent

selected from halogen, hydroxyl, C₁-C₆ alkoxy, C₁-C₆ alkylthio, C₁-C₆ hydroxyalkyl, C₁-C₆ hydroxyalkoxy, C₁-C₆ alkoxycarbonyl, C₃-C₈ cycloalkyl, -NR⁹R¹⁰, -COOR²², -CONR²³R²⁴, -SO₂NR²⁵R²⁶, -NR²⁷SO₂R²⁸ and ZR⁶⁸ or

alternatively, R⁷ and R⁸ may together with the nitrogen atom to which they are

5 attached form a 4- to 7-membered saturated heterocyclic ring that optionally further comprises one or two ring heteroatoms independently selected from nitrogen, oxygen and sulphur and that optionally further comprises a bridging group, the heterocyclic ring being optionally substituted with at least one substituent selected from halogen, hydroxyl, cyano, C₁-C₆ alkyl, C₁-C₆ alkoxy, C₁-C₆ alkylthio, C₁-C₆ hydroxyalkyl, C₁-C₆ hydroxyalkoxy, C₁-C₆ alkoxycarbonyl, C₃-C₈ cycloalkyl, -NR¹¹R¹², -COOR²⁹,
10 -CONR³⁰R³¹, -SO₂NR³²R³³, -NR³⁴SO₂R³⁵, Z'R⁶⁹, (CH₂)₁₋₆NR⁷⁰R⁷¹, SO₂R⁷², NR⁷³CONR⁷⁴SO₂R⁷⁵ or M(CH₂)₁₋₆COOR⁷⁶ wherein M represents a bond, O, S, SO, SO₂, and a group >NR⁷⁷;

R⁹ and R¹⁰ each independently represent hydrogen or a C₁-C₆ alkylcarbonyl,

15 C₂-C₇ alkenyl or C₁-C₇ alkyl group, each group being optionally substituted with at least one substituent selected from hydroxyl, -NR³⁶R³⁷, -COOR³⁸, -CONR³⁹R⁴⁰, -SO₂NR⁴¹R⁴², -NR⁴³SO₂R⁴⁴, C₁-C₆ alkoxy, C₁-C₆ alkylthio, C₁-C₆ alkoxycarbonyl and a saturated or unsaturated 3- to 10-membered ring system which may comprise at least one ring heteroatom selected from nitrogen, oxygen and sulphur, the ring system in turn
20 being optionally substituted with at least one substituent selected from halogen, hydroxyl, oxo, carboxyl, cyano, C₁-C₆ alkyl and C₁-C₆ hydroxyalkyl, or

alternatively, R⁹ and R¹⁰ may together with the nitrogen atom to which they are attached form a 4- to 7-membered saturated heterocyclic ring that optionally further comprises one or two ring heteroatoms independently selected from nitrogen, oxygen and
25 sulphur, the heterocyclic ring being optionally substituted with at least one substituent selected from -OR⁵⁴, -NR⁵⁵R⁵⁶, -(CH₂)_t-NR⁵⁷R⁵⁸ where t is 1, 2, 3, 4, 5 or 6, -COOR⁵⁹, -CONR⁶⁰R⁶¹, -SO₂NR⁶²R⁶³, -NR⁶⁴SO₂R⁶⁵, C₁-C₆ hydroxyalkyl, C₁-C₆ alkoxy, C₁-C₆ alkylthio, C₁-C₆ alkoxycarbonyl and Z''R⁸⁰;

R¹¹ and R¹² each independently represent hydrogen or a C₁-C₆ alkylcarbonyl, C₁-

30 C₆ alkoxycarbonyl, C₂-C₇ alkenyl or C₁-C₇ alkyl group, each group being optionally

substituted with at least one substituent selected from hydroxyl, $-NR^{45}R^{46}$, $-COOR^{47}$, $-CONR^{48}R^{49}$, $-SO_2NR^{50}R^{51}$, $-NR^{52}SO_2R^{53}$, $-NR^{66}C(O)R^{67}$, C_1 - C_6 alkoxy, C_1 - C_6 alkylthio and C_1 - C_6 alkoxycarbonyl;

Z , Z' and Z'' independently represent a bond, O, S, SO, SO_2 , $>NR^{78}$, C_1 - C_6 alkylene,

5 or a group $-O(CH_2)_{1-6}$, $-NR^{79}(CH_2)_{1-6}$ or $-S(O)_p(CH_2)_{1-6}$ wherein p is 0, 1 or 2;

R^{68} , R^{69} and R^{80} independently represent tetrazolyl or a 5- to 6- membered heterocyclic ring comprising from 1 to 4 heteroatoms selected from nitrogen, oxygen and sulphur, which heterocyclic ring is substituted by at least one substituent selected from hydroxyl, $=O$, and $=S$, and which heterocyclic ring may further be optionally substituted
10 by at least one substituent selected from halogen, nitro, cyano, $-SO_2C_{1-6}$ alkyl, C_{1-6} alkoxycarbonyl, and a C_{1-6} alkyl group which C_{1-6} alkyl group can be optionally substituted by at least one substituent selected from halogen and hydroxyl;

R^{13} , R^{14} , R^{15} , R^{16} , R^{17} , R^{18} , R^{19} , R^{20} and R^{21} each independently represent hydrogen or C_1 - C_6 alkyl optionally substituted by at least one substituent selected from hydroxyl,

15 halogen and C_1 - C_6 alkoxy;

R^{22} , R^{23} , R^{24} , R^{25} , R^{26} , R^{27} , R^{28} , R^{29} , R^{30} , R^{31} , R^{32} , R^{33} , R^{34} and R^{35} each independently represent hydrogen or C_1 - C_6 alkyl optionally substituted by at least one substituent selected from hydroxyl, halogen and C_1 - C_6 alkoxy;

R^{36} , R^{37} , R^{38} , R^{39} , R^{40} , R^{41} , R^{42} , R^{43} , R^{44} , R^{45} , R^{46} , R^{47} , R^{48} , R^{49} , R^{50} , R^{51} , R^{52}
20 and R^{53} each independently represent hydrogen or C_1 - C_6 alkyl optionally substituted by at least one substituent selected from hydroxyl, halogen and C_1 - C_6 alkoxy;

R^{54} , R^{55} , R^{56} , R^{57} , R^{58} , R^{59} , R^{60} , R^{61} , R^{62} , R^{63} , R^{64} , R^{65} , R^{66} and R^{67} each independently represent hydrogen or C_1 - C_6 alkyl optionally substituted by at least one substituent selected from hydroxyl, halogen and C_1 - C_6 alkoxy; and

25 R^{70} , R^{71} , R^{72} , R^{73} , R^{74} , R^{75} , R^{76} , R^{77} , R^{78} and R^{79} each independently represent hydrogen or C_1 - C_6 alkyl optionally substituted by at least one substituent selected from hydroxyl, halogen and C_1 - C_6 alkoxy;

with the provisos that:

- (a) when X represents NHC(O) , p is 0, q is 0, n is 1 and R^3 , R^5 and R^6 each independently represent hydrogen, then R^2 is other than a 2-carboxy-phenyl group; and
- (b) when X represents NHC(O) , p is 0, q is 0, n is 2, R^3 represents hydrogen and each R^5 and R^6 independently represents hydrogen, then R^2 is other than a 3,4-diamino-phenyl group or a 5-methyl-2-furanyl group; and
- (c) when X represents C(O)NH , p is 0, q is 0, n is 2, R^3 represents hydrogen and each R^5 and R^6 independently represents hydrogen, then R^2 is other than an unsubstituted phenyl group, an unsubstituted 1H-indol-3-yl group, or a 2-methyl-1H-indol-3-yl group.

2. A compound according to claim 1, wherein X is NHC(O) .

3. A compound according to claim 1 or claim 2, wherein R^2 represents an unsaturated 4-, 5- or 6-membered ring optionally comprising one ring heteroatom selected from nitrogen, oxygen and sulphur, the ring being optionally substituted with one, two, three or four substituents independently selected from halogen, $-\text{COOR}^{13}$, hydroxyl, $-\text{NR}^{14}\text{R}^{15}$, $-\text{CONR}^{16}\text{R}^{17}$, $-\text{SO}_2\text{NR}^{18}\text{R}^{19}$, $-\text{NR}^{20}\text{SO}_2\text{R}^{21}$, $\text{C}_1\text{-C}_4$ alkyl, $\text{C}_1\text{-C}_4$ alkylcarbonyl, $\text{C}_1\text{-C}_4$ alkoxy, $\text{C}_1\text{-C}_4$ alkylcarbonyloxy, $\text{C}_1\text{-C}_4$ alkoxycarbonyl, $\text{C}_1\text{-C}_4$ hydroxyalkyl and $-\text{S(O)}_m\text{C}_1\text{-C}_4$ alkyl where m is 0, 1 or 2.

4. A compound according to any one of the preceding claims, wherein R^3 represents hydrogen or a group $-\text{R}^7$ or $-\text{NR}^7\text{R}^8$.

5. A compound according to any one of the preceding claims wherein R^7 and R^8 each independently represent hydrogen or $\text{C}_1\text{-C}_{10}$ alkyl optionally substituted with one or two substituents independently selected from halogen, hydroxyl, $\text{C}_1\text{-C}_4$ alkoxy, $\text{C}_1\text{-C}_4$ alkylthio, $\text{C}_1\text{-C}_4$ hydroxyalkyl, $\text{C}_1\text{-C}_4$ hydroxyalkoxy, $\text{C}_1\text{-C}_4$ alkoxycarbonyl, $\text{C}_5\text{-C}_6$ cycloalkyl, $-\text{NR}^9\text{R}^{10}$, $-\text{COOR}^{22}$, $-\text{CONR}^{23}\text{R}^{24}$, $-\text{SO}_2\text{NR}^{25}\text{R}^{26}$ and $-\text{NR}^{27}\text{SO}_2\text{R}^{28}$.

6. A compound according to any one of claims 1 to 4, wherein R^7 and R^8 together with the nitrogen atom to which they are attached form a 5- to 6-membered saturated heterocyclic ring that optionally further comprises a ring nitrogen atom, the heterocyclic ring being optionally substituted with one or two substituents independently selected from halogen, hydroxyl, C_1 - C_4 alkoxy, C_1 - C_4 alkylthio, C_1 - C_4 hydroxyalkyl, C_1 - C_4 hydroxyalkoxy, C_1 - C_4 alkoxycarbonyl, C_5 - C_6 cycloalkyl, $-NR^{11}R^{12}$, $-COOR^{29}$, $-CONR^{30}R^{31}$, $-SO_2NR^{32}R^{33}$ and $-NR^{34}SO_2R^{35}$.
7. A compound according to any one of the preceding claims, wherein within each grouping CR^5R^6 , R^5 and R^6 each independently represent hydrogen or C_1 - C_4 alkyl.
8. A compound according to claim 1 selected from:
- 6-Chloro-2-methyl-*N*-[(2*R*)-2-phenylpropyl]-5-quinolinecarboxamide,
 - 6-Chloro-2-methyl-*N*-[(2*S*)-2-phenylpropyl]-5-quinolinecarboxamide,
 - (βR)-*N*-[6-Chloro-2-[methyl[3-(methylamino)propyl]amino]-5-quinolinyl]- β -methyl-benzenepropanamide,
 - (βR)-*N*-[6-Chloro-2-(1-piperazinyl)-5-quinolinyl]- β -methyl-benzenepropanamide,
 - 6-Chloro-2-methyl-*N*-(2-phenylethyl)-5-quinolinecarboxamide,
 - (βR)-*N*-[6-Chloro-2-[3-(ethylamino)propyl]-5-quinolinyl]- β -methyl-benzenepropanamide,
 - (βR)-*N*-[6-Chloro-2-[3-[(3-hydroxypropyl)amino]propyl]-5-quinolinyl]- β -methyl-benzenepropanamide,
 - 3,4-Dichloro- α -methyl-*N*-5-quinolinyl-benzenepropanamide,
 - (βR)-*N*-[6-Chloro-2-[[2-[(2-hydroxyethyl)amino]ethyl]amino]-5-quinolinyl]- β -methyl-benzenepropanamide,
 - 2-Chloro-*N*-[6-chloro-2-(1-piperazinyl)-5-quinolinyl]-benzenepropanamide,
 - 2,4-Dichloro-*N*-[6-chloro-2-(1-piperazinyl)-5-quinolinyl]-benzenepropanamide,
 - 4-Chloro-*N*-[6-chloro-2-(1-piperazinyl)-5-quinolinyl]-benzenepropanamide,

(βR)-*N*-[2-[(3*S*)-3-Amino-1-pyrrolidinyl]-6-chloro-5-quinolinyl]- β -methyl-benzenepropanamide,

N-[6-Chloro-2-(1-piperazinyl)-5-quinolinyl]-2-methoxy-benzenepropanamide,

(βR)-*N*-[6-Chloro-2-[(3*S*)-3-[(3-hydroxypropyl)amino]-1-pyrrolidinyl]-5-quinolinyl]- β -methyl-benzenepropanamide,

(βR)-*N*-[6-Chloro-2-[(3*S*)-3-[(2-hydroxyethyl)amino]-1-pyrrolidinyl]-5-quinolinyl]- β -methyl-benzenepropanamide,

N-[6-Chloro-2-(1-piperazinyl)-5-quinolinyl]-benzenepropanamide,

N-[2-[(3*S*)-3-Amino-1-pyrrolidinyl]-6-chloro-5-quinolinyl]-2-chloro-benzenepropanamide,

2-Chloro-*N*-[6-chloro-2-[(3*S*)-3-[(2-hydroxyethyl)amino]-1-pyrrolidinyl]-5-quinolinyl]-benzenepropanamide,

1-[6-Chloro-5-[[3-(2-chlorophenyl)-1-oxopropyl]amino]-2-quinolinyl]-4-piperidinecarboxylic acid,

2-[(3*S*)-3-Amino-1-pyrrolidinyl]-6-chloro-*N*-[2-(2-chlorophenyl)ethyl]-5-quinolinecarboxamide,

6-Chloro-*N*-[2-(2-chlorophenyl)ethyl]-2-[(3*S*)-3-[(2-hydroxyethyl)amino]-1-pyrrolidinyl]-5-quinolinecarboxamide,

1-[6-Chloro-5-[[[2-(2,6-dichlorophenyl)ethyl]amino]carbonyl]-2-quinolinyl]-4-piperidinecarboxylic acid,

1-[6-Chloro-5-[[[2-(2-chlorophenyl)ethyl]amino]carbonyl]-2-quinolinyl]-4-piperidinecarboxylic acid,

1-[6-Chloro-5-[[[2,2-diphenylethyl]amino]carbonyl]-2-quinolinyl]-4-piperidinecarboxylic acid,

1-[6-Chloro-5-[[[2-(2-phenylethyl)amino]carbonyl]-2-quinolinyl]-4-piperidinecarboxylic acid,

1-[6-Chloro-5-[[[2-(2-fluorophenyl)ethyl]amino]carbonyl]-2-quinolinyl]-4-piperidinecarboxylic acid,

1-[6-Chloro-5-[[[2-(2-methylphenyl)ethyl]amino]carbonyl]-2-quinolinyl]-4-piperidinecarboxylic acid,

1-[6-Chloro-5-[[[(2*S*)-2-phenylpropyl]amino]carbonyl]-2-quinolinyl]-4-piperidinecarboxylic acid,

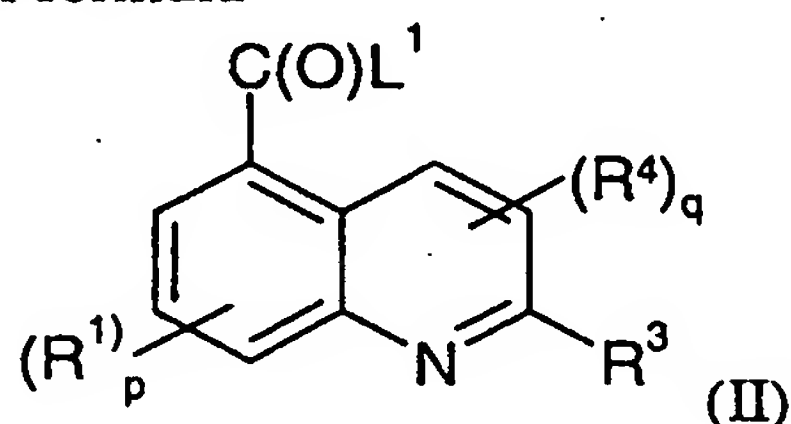
6-Chloro-*N*-[2-(2-chlorophenyl)ethyl]-2-[4-(1,5-dihydro-5-oxo-4*H*-1,2,4-triazol-4-yl)-1-piperidinyl]-5-quinolinecarboxamide, and

5 1-[6-Chloro-5-[[[2-(4-chlorophenyl)ethyl]amino]carbonyl]-2-quinolinyl]-4-piperidinecarboxylic acid,

and all their pharmaceutically acceptable salts and solvates.

10 9. A process for the preparation of a compound of formula (I) as defined in claim 1, or a pharmaceutically acceptable salt or solvate thereof, which comprises

(a) reacting a compound of formula

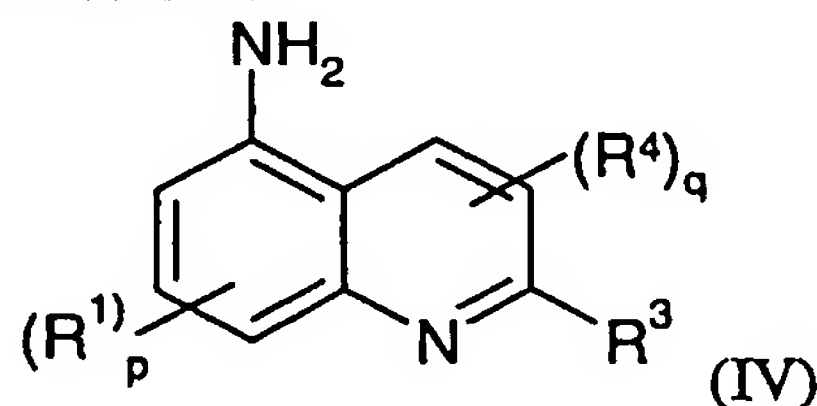


15 wherein L^1 represents a leaving group (e.g. hydroxyl or halogen) and p , q , R^1 , R^3 and R^4 are as defined in formula (I), with a compound of formula



wherein n , R^2 , R^5 and R^6 are as defined in formula (I); or

20 (b) reacting a compound of formula



wherein p , q , R^1 , R^3 and R^4 are as defined in formula (I), with a compound of formula



wherein L^2 represents a leaving group (e.g. hydroxyl or halogen) and n , R^2 , R^5 and R^6 are

25 as defined in formula (I); or

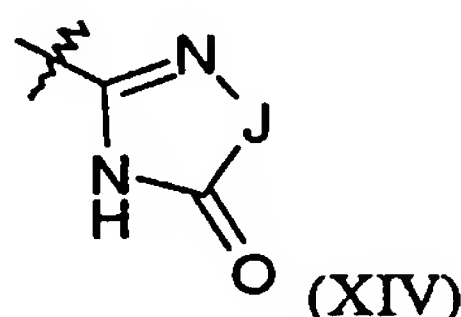
above, followed by an oxidation reaction and then by reaction with a compound of formula (XI) as defined in (e) above under reductive amination conditions; or

- (g) when R^3 represents a group R^7ZR^{68} or NR^7R^8 wherein R^7 and/or R^8 are substituted by a group $Z'R^{69}$ or R^7 and R^8 together with the nitrogen atom to which they are attached form a 4- to 7-membered heterocyclic ring substituted by a group $Z'R^{69}$, and R^{68} or R^{69} is tetrazolyl, reacting a group of formula (XII) or (XIII)



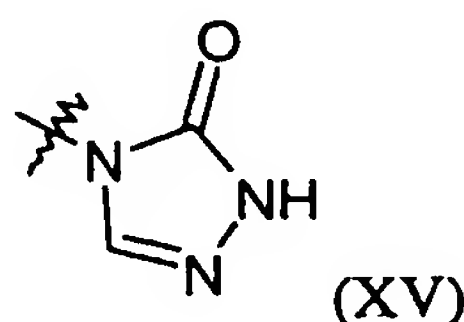
with a compound of formula GN_3 , wherein G is sodium, a trialkylsilyl, an alkyltin or ammonium, to yield a group of formula I wherein R^7 , R^8 , Z, Z' are as defined in formula (I); or

- (h) when R^3 represents a group R^7ZR^{68} or NR^7R^8 wherein R^7 and/or R^8 are substituted by a group $Z'R^{69}$ or R^7 and R^8 together with the nitrogen atom to which they are attached form a 4- to 7-membered heterocyclic ring substituted by a group $Z'R^{69}$, and R^{68} or R^{69} is group of formula

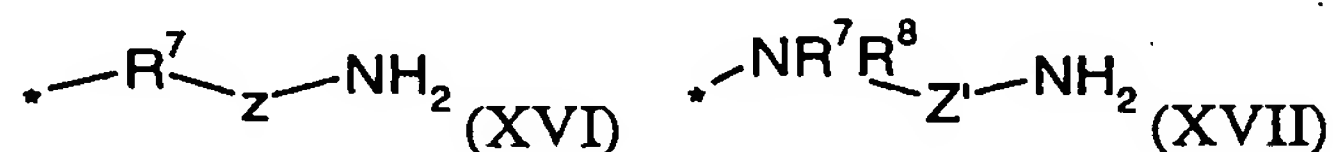


reacting a compound of formula XII or XIII wherein XII or XIII are as defined in (g) above with hydroxylamine, followed by treatment with 1,1'-thiocarbonyldiimidazole and subsequent treatment with silica gives a group of formula (XIV) wherein J is S, alternatively reacting a compound of formula XII or XIII wherein XIII or XIII are as defined in (g) above with hydroxylamine, followed by treatment with a suitable chloroformate gives a group of formula (XIV) wherein J is O; or

- (i) when R^3 represents a group R^7ZR^{68} or NR^7R^8 wherein R^7 and/or R^8 are substituted by a group $Z'R^{69}$ or R^7 and R^8 together with the nitrogen atom to which they are attached form a 4- to 7-membered heterocyclic ring substituted by a group $Z'R^{69}$, and R^{68} or R^{69} is



reacting a compound of formula XVI or XVII



with a source of phosgene followed by treatment with formyl hydrazine and subsequent treatment with base;

and optionally after (a), (b), (c), (d), (e), (f), (g), (h) or (i) carrying out one or more of the following:

- converting the compound obtained to a further compound of the invention
- forming a pharmaceutically acceptable salt or solvate of the compound.

10. A compound of formula (VI) as defined in claim 9.

11. (βR)-*N*-(2,6-Dichloro-5-quinolinyl)- β -methyl-benzenepropanamide.

12. A pharmaceutical composition comprising a compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof as claimed in any one of claims 1 to 8 in association with a pharmaceutically acceptable adjuvant, diluent or carrier.

13. A process for the preparation of a pharmaceutical composition as claimed in claim 12 which comprises mixing a compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof as defined in any one of claims 1 to 8 with a pharmaceutically acceptable adjuvant, diluent or carrier.

14. A compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof as claimed in any one of claims 1 to 8 for use in therapy.

5 15. Use of a compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof as claimed in any one of claims 1 to 8 in the manufacture of a medicament for use in the treatment of rheumatoid arthritis.

10 16. Use of a compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof as claimed in any one of claims 1 to 8 in the manufacture of a medicament for use in the treatment of an obstructive airways disease.

17. Use according to claim 16, wherein the obstructive airways disease is asthma or chronic obstructive pulmonary disease.

15

18. Use of a compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof as claimed in any one of claims 1 to 8 in the manufacture of a medicament for use in the treatment of osteoarthritis.

20 19. Use of a compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof as claimed in any one of claims 1 to 8 in the manufacture of a medicament for use in the treatment of atherosclerosis.

25 20. A method of treating rheumatoid arthritis or osteoarthritis which comprises administering to a patient a therapeutically effective amount of a compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof as claimed in any one of claims 1 to 8.

21. A method of treating an obstructive airways disease which comprises administering to a patient a therapeutically effective amount of a compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof as claimed in any one of claims 1 to 8.